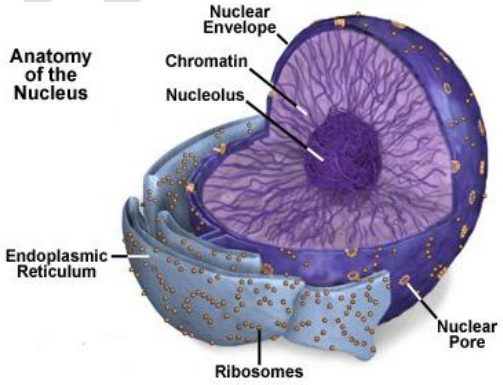
Nucleus

The cell nucleus is a membrane-bound structure that contains a cell's hereditary information and controls its growth and reproduction. It is the command center of a eukaryotic cell and is usually the most notable cell organelle in both size and function.

- ✓ The nucleus (nuclei, plural) the largest component of a cell, frequently appears as rounded, oval, flat, kidney shape, horse shoe shape, segmented or lobulated structure.
- ✓ Position of nucleus often near the center of the cell but in some cells the nucleus located eccentric, basal or peripheral.
- ✓ Found in all eukaryotic cells except mature red blood cells of mammals do not have a nucleus, or are nonnucleated.
- ✓ Most cells have a single nucleus called mononucleated, some cells have two nucleus called binucleated as in liver cells (hepatocyte) or other cells may exhibit multiple nuclei called multinucleated as osteoclast and skeletal muscles.
- ✓ The nucleus stores genetic information. Every cell in the body contains the same genes.
- ✓ The nucleus of a **non dividing** cell (During interphase)consists of the following components:
  1. Nucleolemma or nuclear envelope (karyotheca)
  2. Nuclear sap or karyolymph or nucleoplasm
  3. Chromatin
  4. Nucleolus



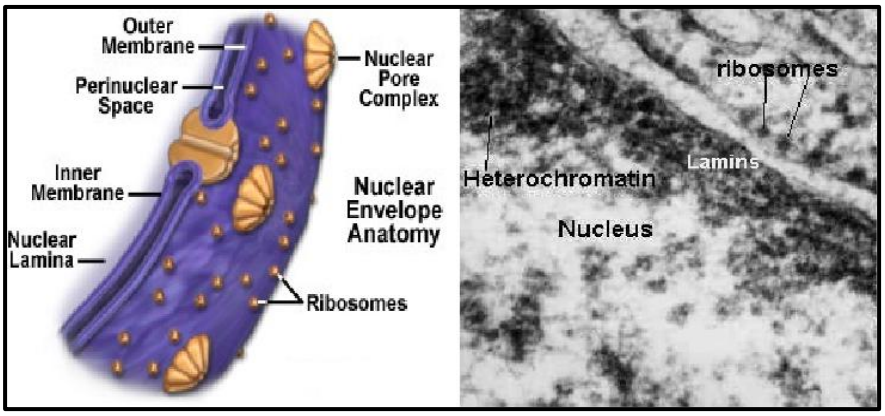
1. Nuclear Envelope or Nuclear Membrane(Karyotheca)

The nuclear envelope forms a selectively permeable barrier (double membrane) between the nucleus and cytoplasmic compartments. The unit membranes of karyotheca are composed of protein and lipid, like plasma membrane.

Electron microscopy reveals that the envelope has two concentric membranes the outer one is called **ectokaryotheca** and inner one is termed **endokaryotheca** separated by a narrow perinuclear space. This space and the outer nuclear membrane are continuous with the extensive cytoplasmic network of the rough endoplasmic reticulum.

Closely associated with the inner nuclear membrane is a highly organized meshwork of proteins called the **nuclear lamina**, which is stabilizes the nuclear envelope. Major components of this layer are the class of intermediate filament proteins called **lamins** that bind to membrane proteins and associate with chromatin in no dividing cells.

The inner and outer nuclear membranes are bridged at nuclear pore complexes. Various core proteins of a nuclear pore complex called **nucleoporins**. Although ions and small solutes pass through the channels by simple diffusion, the pore complexes regulate movement of macromolecules between the nucleus and cytoplasm. Macromolecules shipped out of the nucleus include ribosomal subunits and other RNAs associated with proteins, while inbound traffic consists of chromatin proteins, ribosomal proteins, transcription factors, and enzymes.



Medical Application

Laminopathies," the nuclear envelope is abnormal
Certain mutations in the gene coding for lamin A are associated with a subtype of the disorder progeria, which causes premature aging.

Functions of nuclear envelop are regulate the entry of proteins (histone and hormones) to the nucleus and export of RNAs from nucleus to the cytoplasm. Also encloses the nucleus and separates the genetic material of the cell from the cytoplasm of the cell. And it serves as a barrier to prevent passage of macro-molecules freely between the nucleoplasm and the cytoplasm.

2. Nuclear pores

The nuclear membrane possesses a number of nuclear pores or **annuli**. Various core proteins of a nuclear pore complex, called **nucleoporins**, display eight folds symmetry around the lumen. Although ions and small solutes pass through the channels by simple diffusion, the pore complexes regulate movement of macromolecules between the nucleus and cytoplasm.

The materials exchanged between nucleus and cytoplasm must traverse the nuclear pore complexes. This exchange is very selective and allows passage of only certain molecules of either low or very high molecular weight. The nuclear envelope is a diffusion barrier for ions as small as K^+, Na^+ or Cl^-. On the other hand, very large structures such as ribosomal subunits, which are assembled in the nucleolus, are able to leave the nucleus through the nuclear pore complexes.

3. Chromatin

In non dividing nuclei, chromatin consists of combination of DNA molecules and proteins in a largely uncoiled state**.** Chromatin can coil tightly to form visible chromosomes during cell division. Most of the time the chromatin is uncoiled. Two types of chromatin can be distinguished with both the light and electron microscopes

Heterochromatin (Gr. *heteros* , other +*chroma* , color) appears as coarse, electron-dense material in the electron microscope and as intensely basophilic clumps in the light microscope.

Euchromatin is visible as finely dispersed granular material in the electron microscope and as lightly stained basophilic areas in the light microscope.

The chromatin pattern of a nucleus is a guide to the cell's activity.

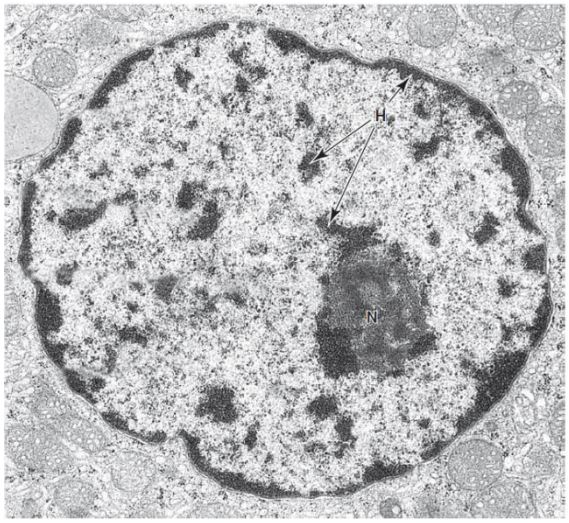
Generally cells with lightly stained nuclei are more active in protein synthesis than those with condensed, dark nuclei. In light-stained nuclei with much euchromatin and few heterochromatic clumps, more DNA surface is available for the transcription of RNA. In dark-stained nuclei rich in highly condensed heterochromatin, the tightly coiled DNA is less accessible for transcription.

- ✓ The extra X chromosome in cells of female mammals forms facultative heterochromatin and can be seen as the Barr body.

DNA in chromatin is extensively packaged by associating with basic proteins called **histones** and with various nonhistone proteins. The structural unit of DNA and histones is the **nucleosome.** These largely form the chromosomes; consist primarily of **histone** and **DNA** in about equal amounts. However, chromosomes also contain non-histone proteins in smaller amounts.

- ✓ Unlike histones (basic), most of the nonhistone proteins are acidic, and they vary qualitatively in different cell types of the same organism.
- ✓ Both histones and nonhistone proteins are synthesized in the cytoplasm and enter the nucleus through the nuclear envelope.
- ✓ Histones are synthesized only when DNA is replicated, whereas nonhistone proteins are synthesized continuously.
- ✓ Histones induce a compact structure in the chromosome.
- ✓ Histones are also considered as stabilizers against heat damage and against nucleases.
- ✓ Activation and repression of genes expression are thought to be carried out by nonhistone proteins.

(This will be discussed in details in molecular biology lectures).



TEM Micrographs of a nucleus

4. Nucleolus

- ✓ Micrographs of a nucleus do show one or more dark regions of the chromatin with spongy appearance. These are nucleoli (sing., **nucleolus**).

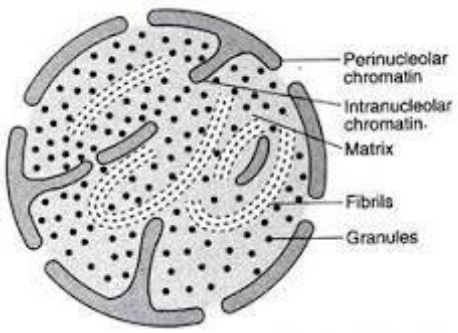
- ✓ The nucleolus is a generally spherical, highly basophilic subdomain of nuclei in cells.
- ✓ The nucleolus is not surrounded by a membrane, it is a densely stained structure found in the nucleus.
- ✓ The intense basophilia of nucleoli is due not to heterochromatin but to the presence of densely concentrated ribosomal RNA (rRNA) that is transcribed, processed, and complexed into ribosomal subunits in nucleoli.
- ✓ Chromosomal regions (satellite stalk of acrocentric chromosomes) with the genes for rRNA organize one or more nucleoli in cells requiring intense ribosome production
- ✓ Molecules of rRNA are processed in the nucleolus and very quickly associate with the ribosomal proteins imported from the cytoplasm via nuclear pore complexes. The newly organized small and large ribosomal subunits are exported back to the cytoplasm through those same nuclear pores.

In eukaryotic cells, nucleolus has a well-ordered structure with four main ultrastructural components. The components can be further identified as:

- **Fibrillar Centers**: It is the place where the ribosomal proteins are formed.
- **Granular Components**: Before ribosomes are formed, these components have rRNA that binds to ribosomal proteins.
- **Dense Fibrillar Components**: It has new transcribed RNA which connects to the ribosomal proteins.

The ultrastructure of the nucleolus can be easily visualized through an electron microscope.

By TEM, an active nucleolus is seen to have **fibrous and granular parts** where rRNA forms and ribosomal subunits are assembled, respectively.



Ultrastructural components of nucleolus

Nucleolus Function

The nucleolus is mainly involved in the production of subunits which then together form ribosomes. Therefore, nucleolus plays an important role in protein synthesis and the production of ribosomes in eukaryotic cells.

5. Nucleoplasm or nuclear sap or karyolymph

- ✓ Chromatin is immersed in a semi fluid medium called the nucleoplasm**.**
- ✓ A difference in pH suggests that nucleoplasm has a different composition from cytoplasm.
- ✓ The nucleus contains a transparent, semi-solid, granular and homogeneous matrix during interphase called as nuclear sap or karyolymph (**enchylema**)
- ✓ karyolymph is a fluid substance containing many particles and network. Primarily it is composed of proteinous material and is the main site for enzyme activity.
- ✓ This nuclear sap also shows variable appearance during different stages of cell division.

Nuclear constituents:

The nucleus contains RNAs, DNA, proteins of two kinds, histone and nonhistone; some lipids; various organic phosphorus compounds; and various inorganic compounds, mostly salts.

Functions of nucleus are:

1. **Cellular regulation:** Houses genetic material, which directs all cellular activities and regulates cellular structure
2. **Production:** Produces ribosomal subunits in nucleolus and exports them into cytoplasm for assembly into ribosomes.

H.W. Why the malignant cells have large nucleoli?